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Purpose/Objective: Precise target definition is of paramount importance in particle therapy. Inflammatory and post surgical alterations may interfere with target contouring. Early response evaluation would be clinically useful but is still problematic. 18F-FDG may not be the optimal radiodrug due to its high uptake in the brain, hindering precise evaluation of skull base invasion, and in inflammatory (post-RT or post surgical) lesions.11C-methionine (MET) PET-CT has been reported as an effective alternative in previous studies thanks to its low uptake in normal brain and its high uptake in salivary gland tumors; however its high uptake in normal salivary gland and in oral mucosa may be a limit.

Materials and Methods: From April 2013 to October 2014, 68 patients affected by head and neck tumors and treated at CNAO with carbon ion radiotherapy have been investigated with MET PET-CT. Histology was: adenoid cystic carcinoma (60 patients), sarcoma (6 patients) mucoepidermoid carcinoma and melanoma (one patient each). Pretreatment MET PET-CT, registered and fused with simulation CT, was employed as a visual aid in target contouring. MR images (T2 weighted, T1 weighted and post contrast T1 weighted) were also used with the same aim. Volumes with methionine uptake comparable with that of parotid glands were included in the high dose CTV; asymmetric findings with uptake intermediate between parotid and brain were included in the low dose CTV. Pre treatment MET failed to show abnormal uptake in 17 patients. In patients with elevated initial uptake a post treatment MET was performed one month after completion of radiotherapy. Pre and post treatment PET is available in 24 patients. The ratio between MET uptake in the treated volume and uptake in the brain (T/B ratio) was calculated pre and post radiotherapy. Dimensional response as detectable at MR has been investigated every 3 months since the end of radiotherapy.

Results: Seventeen patients have shown a decrease of more than 10% in MET uptake after treatment.The tumor to brain ratio has shown a mean reduction of 27%. Post radiotherapy changes had a minimal impact on MET uptake at one month. The mean follow-up was 8 months and the mean volumetric change at the last follow-up was 49%.

Conclusions: MET PET-CT is a useful tool in contouring and early response assessment of head and neck tumors treated with carbon ion radiotherapy. Post RT changes do not mask tumor response. MET uptake decreases significantly even after one month. Longer follow up is needed to correlate early MET PET-CT response with long-term outcome.

PO-0645

Does overall treatment time matter in patients with locally advanced head and neck cancer? An old chestnut revisited

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Purpose/Objective: Treatment for resectable locally advanced head and neck cancers (LAHNC) is generally multimodal, involving surgery followed by radiotherapy (RT) ± chemotherapy (CT) depending on high-risk features such as extracapsular extension (ECE) and R1 resection. The optimal duration of overall treatment time (OTT) has been the subject of much discussion. Accepted wisdom is that the OTT should not exceed 100 days measured from the day of surgery to the end of adjuvant therapy. We questioned whether this was still true in an era of intensified treatment or whether further survival or locoregional control benefits could be obtained by using a shorter OTT.

Materials and Methods: This analysis includes 272 pts. (med. F/U 23.9 mo.) with LAHNC (106 oropharynx, 43 larynx/hypopharynx, 75 oral cavity, 18 nasal/paranasal sinus, 30 unknown primary/other) treated adjuvantly with RT +/- platinum based CT depending on pathological risk factors (Gregoire et al 2010). CT was given at a dose of 100mg/ m^2 q21 days or 30 mg/m^2 weekly. All pts. had IMRT, 2 Gy/ fraction to a total dose of 60-66 Gy. Of the 272 pts. 64 (24%) had ECE and 201 (74%) were R0 status.

Pts. were followed at regular intervals with a clinical examination, flexible endoscopy and imaging. Toxicity was scored according to the RTOG acute radiation morbidity criteria and the RTOG/EORTC late radiation morbidity criteria..

The clinical impact of OTT was assessed using the Kaplan-Meier and Multivariate Cox regression analysis (MVA). Recursive partitioning analysis (RPA) was performed to predict an optimal OTT with regard to clinical outcome.

Results: 223 (82%) pts. had their treatment delivered in <100 days; 49 (18%) had a duration of ≥ 100 days. Baseline characteristics were similar for both groups. MVA identified R1 status (HR 2.2) vs R0 status (p=0.36) but not OTT ≥100 days as an adverse risk factor (ARF) for disease-fre survival (DFS). OTT ≥100 days (HR 4.1 vs 100 days; p=0.00007), R1 status (HR 2.1 vs R0; p=0.04), and ECE (HR 2.3 vs no ECE; p=0.0342) were identified as ARFs for overall survival (OS). The RPA tree identified OTT <87 days as a high-performance group and OTT ≥87 days as the low-performance group for DFS. 95 pts. completed their treatment within 87 days and 110 in ≥87 days. There was no difference in the baseline characterstics.

MVA identified OTT of ≥87 days from surgery to end of RT (HR 2.2 vs <87 days) and R1 status (HR 2.3 vs R0) as ARFs for DFS.

This analysis found the ARFs for OS to be ≥87 days from surgery to end of RT (HR 3.3; p=0.0025 vs <87 days) and ECE (HR 2.6 vs no ECE; p=0.0133). Adverse events did not differ between the groups.

Conclusions: The present analysis has shown that OTT can be an important factor in DFS. OTT of 87 days is challenging and requires careful coordination of procedures and disciplines between surgery and adjuvant therapy, as well as minimizing treatment delays during RT. Our findings suggest that treatment completed within as short a timeframe as possible appears to be associated with longer DFS and that this should be a goal. Further studies are needed to confirm these findings.

PO-0646

Adaptive and robust FDG-PET-based dose painting by numbers (DPBN) in head and neck tumors: a methodological approach

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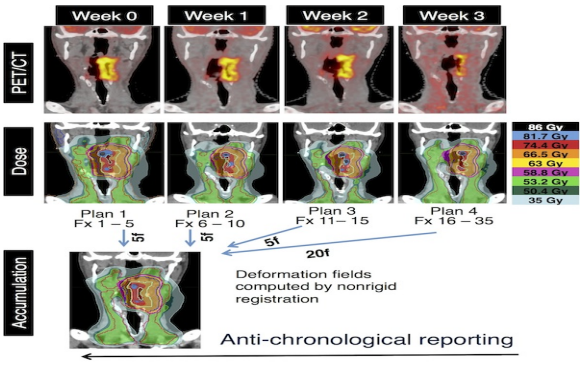
Purpose/Objective: To develop a methodology for using FDG PET/CT in adaptive DPBN in locally advanced head and neck squamous cell carcinoma (HNSCC) patients. Issues related to noise in PET and robustness against geometric errors are addressed.

Materials and Methods: Five patients with locally advanced HNSCC scheduled for chemo-radiotherapy were imaged with FDG-PET/CT at baseline and after 5, 10 and 15 fractions of RT (2 patients were re-imaged only twice). The GTV_{PET} was segmented with a gradient-based method. A double median filter reduces the impact of noise in the conversion from PET uptake to prescribed dose. Filtered FDG uptake values were linearly converted into a voxel-by-voxel prescription from 70 (median uptake) to 86 Gy (highest uptake). To be robust against geometrical uncertainties, a PTV_{PET} was obtained by applying a dilation of 2.5 mm to the entire prescription. Seven iso-uptake thresholds led to 7 sub-levels compatible with the Tomotherapy HiArt® Treatment Planning System. Planning aimed to deliver a median dose of 56 Gy and 70 Gy in 35 fractions on the elective and therapeutic PTVs, respectively. Plan quality was assessed with quality-volume histogram (QVH) and quality factor (QF, objective: <5%). For organs at risk (OARs), DVH constraints were the following: D_{mean} < 26-30 Gy for parotid glands, D_2 < 30 Gy for PRV spinal cord and brain stem. At each time point, plans were generated using a 1 cm collimator width with a total of 3 to 4 plans for each patient. Deformable image registration was used for automatic propagation of volumes of interest and dose summation of the 3 or 4 treatment plans (MIM vista®) (see figure). Finally, to simulate a treatment that is adaptive to anatomical evolution seen at CT but blind to changes in the PET signal, the pre-treatment dose map was deformed and assessed with QVHs on each per-treatment CT scan after non-rigid image registration.



Results: GTV_{PET} segmentations were performed successfully until week 2 of RT but failed in 2 patients at week 3. QVH analysis showed high conformity for all plans (mean $V_{Q=0.95}$ 93%; mean $V_{Q=1.05}$ 3.9%; mean QF 2.2%) demonstrating feasibility of the treatment. Good OAR sparing was achieved while keeping high plan quality (see table). When comparing biologic/anatomic adaptation versus only anatomic adaptation, QFs were improved in all cases (range 0.8 – 3.7%) with a median value of 2.1% and 4.7% for the biological adaptive and anatomic only adaptive strategy, respectively.

Table. Dose/volume parameters (Mean±SD) for targets and organs-at-risk for pre-treatment dose and dose accumulation reported in pre-treatment volumes

Target	Pretreatment dose (Gy)	Accumulated dose (Gy)
GTV_{PET}		
D2%	86.2 ± 0.6	83.9 ± 1.8
D50%	75.3 ± 1.5	73.0 ± 0.4
D95%	70.1 ± 0.2	69.9 ± 0.6
PTV70		
D2%	78.8 ± 2.4	76.4 ± 1.3
D50%	70.0 ± 0.1	69.9 ± 0.1
D95%	68.3 ± 0.5	67.5 ± 0.4
PTV56		
D2%	72.9 ± 1.8	72.0 ± 1.3
D50%	57.0 ± 1.2	57.1 ± 2.0
D95%	54.8 ± 0.4	54.1 ± 0.9
Ipsi parotid		
Dmean	27.4 ± 1.1	26.1 ± 1.2
Contra parotid		
Dmean	22.7 ± 1.2	21.9 ± 2.0
PRV SC		
D2%	27.2 ± 0.8	26.6 ± 0.3
PRV BS		
D2%	22.5 ± 2.0	21.0 ± 3.1
Mandibule		
D5%	63.1 ± 6.6	62.4 ± 5.8
QVH		
V(Q=0.95)	95.5 ± 2.2	79.4 ± 1.9
V(Q=1.05)	3.3 ± 1.3	6.3 ± 5.4
QF	1.9 ± 0.2	3.5 ± 0.5

Conclusions: Our results show that adaptive FDG-PET-based escalated dose painting in patients with locally advanced